Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A method for making a cytotoxic mutant protein or pool of proteins from a cytotoxic wild type protein, said mutant protein or pool of proteins having ~~a different~~ receptor-binding specificity for a receptor that is different from the receptor to which ~~than~~ the wild type protein has receptor binding specificity, comprising:

(A) selecting a heteromeric protein toxin having a toxic domain or subunit and a binding domain or subunit, wherein the heteromeric protein toxin is a ribosome inactivating protein;

(B) incorporating mutations into DNA encoding the binding domain or subunit of the heteromeric protein toxin to produce a plurality of variant forms of the heteromeric protein toxin;

(C) generating a library of microorganism clones producing variant forms of the heteromeric protein toxin;

(D) screening the variant forms of the heteromeric protein toxin of said library against a population of screening cells by (i) isolating clones or pools of clones producing said variant forms of the heteromeric protein toxin, (ii) treating preparations of said population of screening cells with variant forms of the heteromeric protein toxin produced by the isolated clones or pools of clones, (iii) observing the treated preparations of said population of screening cells for toxicity, and (iv) selecting based on the observation of toxicity a cytotoxic mutant protein or pool of cytotoxic mutant proteins that inhibits or kills said population of screening cells to a greater extent than the wild-type cytotoxic protein, whereby said selected mutant protein or pool of proteins has the ~~a~~ different receptor binding specificity ~~than the wild-type binding protein~~, wherein the screening cells are insensitive to the selected cytotoxic heteromeric protein toxin at a concentration used in the screening; and

(E) making additional copies of the selected cytotoxic mutant protein or pool of proteins.

2. (previously presented) The method of claim 1, wherein the cells in the population of screening cells are eukaryotic.

3. (original) The method as claimed in claim 1, wherein said library comprises bacteria or bacterial supernatants containing said variant protein toxins.

4. (original) The method as claimed in claim 1, wherein said library comprises yeast or yeast supernatants containing said variant protein toxins.

5. (previously presented) The method as claimed in claim 1, wherein said binding domain or subunit DNA is in a plasmid in said microorganism.

6. (previously presented) The method of claim 1, wherein said mutation is incorporated into said binding domain or subunit by use of a combinatorial cassette method comprising:

(A) preparing synthetic mutant oligonucleotides capable of annealing with a corresponding wild type oligonucleotide from said binding domain or subunit;

(B) annealing said synthetic oligonucleotide from said binding domain or subunit to an overlapping wild type oligonucleotide to form a double stranded sequence;

(C) creating a combinatorial cassette by mutually primed synthesis of said double stranded sequence; and

(D) incorporating said cassette into a vector containing a gene for said toxin.

7. (previously presented) The method as claimed in claim 1 wherein said mutation is incorporated into said binding domain or subunit by means of a unique site elimination method.

8. (canceled)

9. (previously presented) The method as claimed in claim 1 wherein said heteromeric protein toxin is selected from the group consisting of Shiga toxin, Shiga-like toxins, ricin, abrin, gelonin, crotin, pokeweed antiviral protein, saporin, momordin, modeccin, sarcin, diphtheria toxin and Pseudomonas aeruginosa exotoxin A.

10. (original) The method as claimed in claim 9 wherein said heteromeric protein toxin is Shiga toxin or Shiga-like toxin 1.

11. (previously presented) The method as claimed in claim 10 wherein said mutation is incorporated into loop regions at residues 15-19, 30-33 or 58-64.

12. (previously presented) The method as claimed in claim 10 wherein said mutation is incorporated into loop regions at residues 15-19 or 30-33.

13. (previously presented) The method as claimed in claim 2 wherein the cells in the population of screening cells are tumour cells.

14. (previously presented) The method of claim 13 wherein the tumour cells are breast cancer cells.

15. (original) The method as claimed in claim 14 wherein said breast cancer cell is SKBR-3 or CAMA-I.

16. (previously presented) The method as claimed in claim 1 wherein said binding domain or subunit is derived from the B-subunit template of either Shiga toxin or Shiga-like toxins, or homologous counterparts from *E. coli* heat labile enterotoxins, cholera toxin, pertussis toxin or the receptor binding domain of ricin.

17. (previously presented, withdrawn) A method of killing or inhibiting a target cell comprising treating said target cell with a cytotoxic mutant protein or pool of proteins made in accordance with the method of claim 1, wherein said target cell expresses a receptor to which the cytotoxic mutant protein or pool of proteins specifically binds.

18. (previously presented, withdrawn) A method for identifying therapeutic proteins having binding specificity for a target cell, comprising:

(A) making a cytotoxic mutant protein or pool of proteins by the method as claimed in claim 1; and

(B) screening said cytotoxic mutant protein or pool of proteins against said target cells and against non-target cells by treating a preparation of target and a preparation of non-target cells with said cytotoxic mutant protein or pool of proteins, and selecting a therapeutic protein or pool of therapeutic proteins that are effective to inhibit or kill said target cells and that are less effective at inhibiting or killing said non-target cells than at inhibiting or killing said target cells.

19. (canceled)

20. (previously presented, withdrawn) A method for constructing diagnostic probes as claimed in claim 28 wherein said marker DNA codes for green-fluorescent protein (GFP).

21-23. (canceled)

24. (previously presented, withdrawn) A method for treating a condition requiring targeting a medicine to a target cell occurring in a host organism comprising selecting a medicament by the method as claimed in claim 32 and administering to said host organism an effective amount of said medicament.

25. (previously presented, withdrawn) A method for treating a condition requiring targeting a medicine to a target cell occurring in a host organism comprising selecting a medicament by the method as claimed in claim 33, and administering to said host organism an

effective amount of said medicament.

26. (canceled)

27. (previously presented, withdrawn) A method for constructing a diagnostic probe for detecting the presence of a cell surface marker comprising:

(A) selecting a cytotoxic mutant protein that specifically binds to the cell surface marker by the method as claimed in claim 1; and

(B) preparing a diagnostic probe by labeling the selected cytotoxic mutant protein in a manner which maintains the ability of the binding domain or subunit of the selected cytotoxic mutant protein to specifically bind to the cell surface marker.

28. (previously presented, withdrawn) The method of claim 27, wherein the diagnostic probe is prepared by a method comprising:

(i) preparing a diagnostic DNA sequence comprising a marker DNA encoding a detectable marker and a binding domain or subunit DNA sequence encoding the binding domain or subunit of the selected cytotoxic mutant protein; and

(ii) expressing the diagnostic DNA sequence to generate a diagnostic probe.

29. (previously presented, withdrawn) The method of claim 27, further comprising the step of modifying the cytotoxic mutant protein or pool of proteins by dissociation or inactivation of the toxic domain or subunit of the cytotoxic mutant protein.

30-31. (canceled)

32. (currently amended, withdrawn) A method for making a targeted medicament for delivery to a target cell having a cell surface marker, said targeted medicament comprising a binding portion and a medicament portion comprising the step of:

(A) identifying a binding subunit which binds to the cell surface marker by a process comprising the steps of

(i) selecting a heteromeric protein toxin having a toxic domain or subunit and a binding domain or subunit, wherein the heteromeric protein toxin is a ribosome inactivating protein;

(ii) incorporating mutations into DNA encoding the binding domain or subunit of the heteromeric protein toxin to produce a plurality of variant forms of the heteromeric protein toxin;

(iii) generating a library of microorganism clones producing variant forms of the heteromeric protein toxin;

(iv) screening the variant forms of the heteromeric protein toxin of said library against a population of screening cells by (a) isolating clones or pools of clones producing said

variant forms of the heteromeric protein toxin, (b) treating preparations of said population of screening cells with variant forms of the heteromeric protein toxin produced by the isolated clones or pools of clones, (c) observing the treated preparations of said population of screening cells for toxicity, and (d) selecting based on the observation of toxicity a cytotoxic mutant protein or pool of cytotoxic mutant proteins that inhibits or kills said population of screening cells to a greater extent than the wild-type cytotoxic protein, whereby said selected mutant protein or pool of proteins has ~~a different~~ receptor-binding specificity for a receptor that is different from the receptor to which ~~than~~ the wild type protein has receptor binding specificity, wherein the screening cells are insensitive to the selected wild-type heteromeric protein toxin at a concentration used in the screening; and

(v) determining the sequence of the binding domain or subunit of the selected cytotoxic mutant protein for use as the binding portion of the targeted medicament; and

(B) combining the binding portion with the medicament portion.

33. (previously presented, withdrawn) The method of claim 32, wherein the binding portion and the medicament portion are combined by preparing a medicament DNA sequence comprising a medicinal DNA encoding a medicinal polypeptide for use as the medicament portion, and a binding domain or subunit DNA sequence encoding the binding portion, further comprising the step of expressing the medicament DNA sequence.

34-36 (canceled)

37. (currently amended, withdrawn) A method for making a nucleic acid sequence, or pool of nucleic acid sequences, encoding a cytotoxic mutant protein, or pool of cytotoxic mutant proteins, of a cytotoxic wild type protein said mutant protein or pool of proteins having ~~a different~~ receptor-binding specificity for a receptor that is different from the receptor to which ~~than~~ the wild type protein has receptor binding specificity, comprising:

(A) selecting a heteromeric protein toxin having a toxic domain or subunit and a binding domain or subunit, wherein the heteromeric protein toxin is a ribosome inactivating protein;

(B) incorporating mutations into DNA encoding the binding domain or subunit of the heteromeric protein toxin to produce a plurality of variant forms of the heteromeric protein toxin;

(C) generating a library of microorganism clones producing variant forms of the heteromeric protein toxin;

(D) screening the variant forms of the heteromeric protein toxin of said library against a population of screening cells by (i) isolating clones or pools of clones producing said variant forms of the heteromeric protein toxin, (ii) treating preparations of said population of screening cells with variant forms of the heteromeric protein toxin produced by the isolated clones or pools of clones, (iii) observing the treated preparations of said population of screening

cells for toxicity, and (iv) selecting based on the observation of toxicity a cytotoxic mutant protein or pool of cytotoxic mutant proteins that inhibits or kills said population of screening cells to a greater extent than the wild-type cytotoxic protein, whereby said selected mutant protein or pool of proteins has the ~~a~~ different receptor binding specificity ~~than the wild-type binding protein~~, wherein the screening cells are insensitive to the selected wild-type cytotoxic heteromeric protein toxin at a concentration used in the screening; and

(E) making additional copies of the nucleic acid sequence or pool of nucleic acid sequence encoding the selected cytotoxic mutant protein or pool of cytotoxic mutant proteins.

38. (previously presented, withdrawn) The method of claim 37, wherein the cells in the population of screening cells are eukaryotic.

39. (previously presented, withdrawn) The method of claim 38, wherein the cells in the population of screening cells are tumor cells.

40. (previously presented, withdrawn) The method of claim 39, wherein the tumor cells are breast cancer cells.

41. (previously presented, withdrawn) The method of claim 37, wherein the binding domain or subunit is derived from the B-subunit of either Shiga toxin and Shiga-like toxins, or homologous counterparts from *E. coli* heat labile enterotoxins, cholera toxin, pertussis toxin or the receptor binding domain of ricin.

42. (canceled)

43. (previously presented) The method of claim 1, wherein in step B the mutations are randomly incorporated into the DNA encoding the binding domain or subunit of the heteromeric protein toxin.